

Form PTO-1449 **U.S. Department of Commerce**  
**Patent and Trademark Office**

Atty. Docket No.  
59472-A-PCT-US

Serial No.  
10/049,893

SEP 25 2002  
**INFORMATION DISCLOSURE CITATION**  
Use several sheets if necessary)

Applicants  
David Stern, et al.

Filing Date  
February 13, 2002

Group Art Unit

### U.S. PATENT DOCUMENTS

Examiner Initials	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
<i>JAE</i>	US 5 8 6 4 0 1 8	4/16/96	Morser et al.			

### FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation	
					Yes	No
<i>JAE</i> WO 9 7 3 9 1 2 5	10/23/97	Europe				

### OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

<i>JAE</i>	Akama, T. Keith, et al., "Amyloid $\beta$ -peptide stimulates nitric oxide production in astrocytes through an NgkB-dependent mechanism," <u>Proc. Natl. Acad. Sci.</u> , 1998, 95: 5795-5800 ( <b>Exhibit 3</b> );
	Behl, C., et al., "Hydrogen Peroxide Mediates Amyloid $\beta$ Protein Toxicity", <u>Cell</u> , 1994, 77: 817-827 ( <b>Exhibit 4</b> );
	Combs, K. Colin, et al. "Identification of Microglial Signal Transduction Pathways Mediating a Neurotoxic Response to Amyloidogenic Fragments of $\beta$ -Amyloid and Prion Proteins", <u>Journal of Neuroscience</u> , 1999, 19(3): 928-939 ( <b>Exhibit 5</b> );
	Forloni, Gianluigi, et al. "Amyloid in Alzheimer's Disease and Prior-Related Encephalopathies: Studies With Synthetic Peptides", <u>Progress in Neurobiology</u> , 1996, 49: 287-315 ( <b>Exhibit 6</b> );
	Ghiso, Jorge, et al. "Unifying Features of Systemic and Cerebral Amyloidosis", <u>Molecular Neurobiology</u> , 1994, 8(1): 49-64 ( <b>Exhibit 7</b> );
	Inagaki, Fuyuhiko, et al. "Conformation of Erabutoxins a and b in Aqueous Solution as Studied by Nuclear Magnetic Resonance and Circular Dichroism", 1978, 89: 433-443 ( <b>Exhibit 8</b> ); <b>Need magazine article #26</b>
	Kilsilevsky, Robert, et al. "Arresting amyloidosis in vivo using small-molecule anionic sulphonates or sulphates: implications for Alzheimer's disease", <u>Nature Medicine</u> , 1995, 1: 143-148 ( <b>Exhibit 9</b> );
	Kimball, M.R., et al. "Molecular Conformation of Erabutoxin b; Atomic Coordinates At 2.5 Å Resolution", <u>Biochemical and Biophysical Research Communication</u> , 1979, 88: 950-959 ( <b>Exhibit 10</b> );
<i>JAE</i>	Kindy, S. Mark and Rader, J. Daniel "Reduction in Amyloid A Amyloid Formation in Apolipoprotein-E-Deficient Mice", <u>American J. Pathology</u> , 1998, 152: 1387-1395 ( <b>Exhibit 11</b> );

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DATE CONSIDERED

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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

*WG* Kirschner, A. Daniel, et al. "X-ray diffraction from intraneuronal pairs helical filaments and extraneuronal amyloid fibers in Alzheimer disease indicates cross- $\beta$  conformation", Proc. National Acad. Sci., 1986, 83: 503-507 (**Exhibit 12**);

Lander, H. L., et al. "Activation of the Receptor for Advanced Glycation Endproducts triggers a MAP Kinase pathway regulated by oxidant stress", J. Biol. Chem., 1997, 272: 17810-17814 (**Exhibit 13**);

Levine, Harry "Thioflavine T interaction with synthetic Alzheimer's disease  $\beta$ -amyloid peptides: Detection of amyloid aggregation in solution", Protein Sci., 1993, 2(3): 404-410 (**Exhibit 14**);

Mattson, M.P. and Goodman, Y. "Different amyloidogenic peptides share a similar mechanism of neurotoxicity involving reactive oxygen species and calcium", Brain Res., 1995, 676: 219-224 (**Exhibit 15**);

Pike, J. Christian, et al. "Neurodegeneration Induced by  $\beta$ -Amyloid Peptides in vitro: The Role of Peptide Assembly State", J. Neuroscience., 1993, 13(4): 1676-1687 (**Exhibit 16**);

Prusiner, B. Stanley, et al. "Prion Protein Biology", Cell, 1998, 93: 337-348 (**Exhibit 17**);

Serpell, L.C., et al. "The molecular basis of amyloidosis", Cellular and Molecular Life Sci., 1997, 53: 871-887 (**Exhibit 18**);

Sipe, D. Jean, et al.) "Characterization of the Inbred CE/J Mouse Strain as Amyloid Resistant", Am. J. of Pathology, 1993, 143: 1480-1485 (**Exhibit 19**);

Sipe, D. Jean "Amyloidosis", Ann. Review of Bioche., 1992, 61: 947-975 (**Exhibit 20**);

Smith, M.A. et al. "Heme oxygenase-1 is associated with the neurofibrillary pathology of Alzheimer's Disease", Am. J. Pathol., 1994, 145(1): 42-47 (**Exhibit 21**);

Soto, Claudio and Castano, M. Eduardo "The conformation of Alzheimer's  $\beta$  peptide determines the rate of amyloid formation and its resistance to proteolysis", Biochemical J., 1996, 314: 701-707 (**Exhibit 22**);

Soto, Claudio, et al. "Apolipoprotein E increases the fibrillogenic potential of synthetic peptides derived from Alzheimer's, Gelsolin and AA amyloids", 1995, FEBS Letters, 1995, 371: 110-114 (**Exhibit 23**);

Strauss, Sylvia, et al. "Detection of Interleukin-6 and  $\alpha_2$ -Macroglobulin Immunoreactivity in Cortex and Hippocampus of Alzheimer's Disease Patients", J. Acad. of Pathology., 1992, 66(2): 223-230 (**Exhibit 24**);

Yan S-D, Chen X, Chen M, Zhu H, Roher A, Slattery T, Zhao L, Nagashima M, Morser J, Migheli A, Nawroth P, Stern DM, Schmidt "A-M: RAGE and amyloid-beta peptide neurotoxicity in Alzheimer's disease", Nature, 1996, 382: 685-691 (**Exhibit 25**);

Yan, Shi Du, et al. "Amyloid- $\beta$  peptide-Receptor for Advanced Glycation End product interaction elicits neuronal expression of macrophage-colony stimulating factor: A proinflammatory pathway in Alzheimer disease", Proceedings of the Nat. Acad. Sci., 1997, 94: 5296-5301 (**Exhibit 26**); and

Yankner, A. Bruce "Mechanisms of Neuronal Degeneration in Alzheimer's Disease", Neuron, 1996, 16: 921-932 (**Exhibit 27**).

EXAMINER

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**INFORMATION DISCLOSURE STATEMENT**  
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Application Number	10/049,893
Filing Date	July 22, 2002
First Named Inventor	David Stern, et al.
Art Unit	
Examiner Name	
Attorney Docket No.	59472-A-PCT- US/JPW/AJM/JCS

**U.S. PATENT DOCUMENTS**

Examiner Initials <sup>*</sup>	Cite No. <sup>1</sup>	Document Number Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document

**FOREIGN PATENT DOCUMENTS**

Examiner Initials <sup>*</sup>	Cite No. <sup>1</sup>	Foreign Patent Document Country Code*Number*Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	T <sup>6</sup>
<i>AE</i>		WO 99/18987	4/22/1999	The Trustees of Columbia University in the City of New York	
<i>↓</i>		WO 97/26913	7/31/1997	The Trustees of Columbia University in the City of New York	
<i>↓</i>		WO 95/20979	8/10/1995	The Picower Institute for Medical Research	

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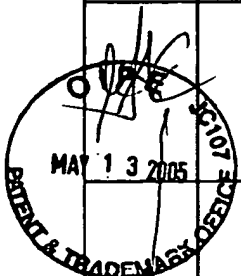
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Applicants: Stern, et al.  
Serial No. : 10/049,893  
Filed: July 22, 2002  
Exhibit 1

<b>Form PTO-1449</b> <b>U.S. Department of Commerce</b> <b>Patent and Trademark Office</b>  <b>INFORMATION DISCLOSURE CITATION</b> (Use several sheets if necessary)	Application Number	10/049,893
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### NON PATENT LITERATURE DOCUMENTS

Examiner Initials <sup>1</sup>	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		February 21, 2005 Communication enclosing a Supplementary Partial European Search Report issued in connection with related European Patent Application No. 00955464.3, on behalf of The Trustees of Columbia University in the City of New York, regional stage of PCT International Application No. PCT/US00/22059, filed August 11, 2000	
		Zhu, et al., "RAGE interaction with Abeta fibrils activates signal transduction mechanisms and results in apoptosis activation of MAP kinases and nuclear translocation of NF-EkB," Society for Neuroscience Abstracts 24: 228 (1998)	
		Yan, et al., "RAGE and Amyloid-Beta Peptide Neurotoxicity in Alzheimer's Disease," Nature: 382: 685-691 (1996)	
		Yan, et al., "Cellular cofactors potentiating induction of stress and cytotoxicity by amyloid beta-peptide," Biochimica Et Biophysica Acta. Molecular Basis of Disease 1502: 145-157 (2000)	
		Yan, et al., "Receptor-dependent cell stress and amyloid accumulation in systemic amyloidosis," Nature Medicine 6: 643-651 (2000)	
		Sousa, et al., "Interaction of the receptor for advanced glycation endproducts (RAGE) with transthyretin triggers nuclear transcription factor kB (NF0kB) activation," Laboratory Investigation 80: 1101-1110 (2000)	

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 Exhibit I